

# Increasing Awareness on Racial Disparities in Liver Transplantation for Hepatocellular Carcinoma in the United States

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**H**epatocellular carcinoma (HCC) is one of the fastest rising causes of cancer-related death in the United States, having tripled in incidence since the early 1980s.<sup>(1)</sup> Blacks and Hispanics are the two ethnic groups that have the largest increase in incidence but continue to have the lowest rates of curative HCC treatment.<sup>(2)</sup> Multiple studies of population-based cohorts and center-specific cohorts have explored some of the reasons for racial disparities in HCC treatment and outcomes over the past 2 decades, yet the disparities continue to persist.

Curative therapies for HCC include resection, ablation, and liver transplantation. Of all these therapies, liver transplant is perhaps one of the most

difficult for patients to attain, not only because of the impact of comorbidities and long wait times resulting in tumor progression before transplant but also because of the impact of social situations. Organ transplantation is one of the few medical therapies impacted by the need for abstinence from alcohol and illicit drugs, compliance with medical appointments and recommendations, adequate insurance for medical and surgical care, and social support for both pretransplant and posttransplant care. Because of the imbalance between the supply of donor organs and the demand of waiting patients, transplant centers have an ethical obligation to list patients who will have good long-term outcomes after transplantation.

Racial inequity in the United States refers to the social, financial, and structural disparities that affect different races within the United States. These inequities may be manifested in the distribution of wealth, power, and life opportunities afforded to people based on their race or ethnicity, both historic and modern. Health care disparity in racial and ethnic groups has long been described in the literature. These disparities have been elusive to determining the underlying causes but have continued to be an important element to study. Beginning in 2002, the Agency for Healthcare Research and Quality (AHRQ) was charged by the United States Department of Health and Human Services to publish a yearly report on national health care quality and disparities.<sup>(3)</sup> As per the 2017 report by AHRQ, overall some disparities decreased from 2000 to 2014-2015, but disparities persist, especially for poor and uninsured populations in all priority areas.<sup>(3)</sup> For instance, 40% of quality measures are worse for black patients than white patients in the United States. One study estimated that if the disparities in health care were eliminated, direct costs of medical care could be reduced by \$230 billion and indirect costs associated with illness and premature

*Abbreviation: HCC, hepatocellular carcinoma.*

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death could be reduced by more than \$1 trillion over a 3-year time period.<sup>(4)</sup> However, in order to reduce or eliminate racial disparities, we must first understand the underlying causes of the disparities.

In this issue of *Hepatology Communications*, Dakhouli et al.<sup>(5)</sup> report results of their detailed analysis of liver transplantation for HCC at Indiana University. The authors manually extracted data from medical charts of 1,032 (86%) white and 164 (14%) black patients with HCC treated at their center between January 2000 and June 2014 in an attempt to elucidate reasons for lower rates of orthotopic liver transplantation (OLT) among black patients with HCC. Each patient was reviewed, and data were collected on demographics, comorbidities, tumor characteristics, underlying liver disease etiology and stage, and treatment modalities received throughout the disease course as well as insurance status and social information, such as alcohol and substance abuse. Because of the nature of this review, the authors were also able to perform a subgroup analysis on patients who were potential liver transplant candidates based on tumor stage but who did not undergo liver transplant in order to identify causes for failure to receive a transplant. Black patients were matched to white patients by age ( $\pm 3$  years) and sex in a 1:1 ratio.

Black patients with HCC were significantly younger (59.7 years versus 62.0 years;  $P = 0.005$ ) with lower body mass index (BMI) (27.4 kg/m<sup>2</sup> versus 29.0 kg/m<sup>2</sup>;  $P = 0.001$ ) than white patients and had more hypertension (64% versus 54%;  $P = 0.02$ ). Other comorbidities were similar between the two groups. Black patients also had more hepatitis C and/or alcohol as underlying liver disease etiology compared to white patients (77% versus 49%;  $P < 0.001$ ). Interestingly, while black patients presented with a more advanced tumor-node-metastasis stage of HCC, there was no difference in the distribution of Barcelona Clinic Liver Cancer stage; in addition, the number of patients who presented within the Milan criteria (one lesion  $< 5$  cm or up to three lesions all  $< 3$  cm, without vascular invasion or extrahepatic spread) was similar between black and white patients (42% versus 48%;  $P = 0.19$ ). Despite similar tumor staging at diagnosis, the authors found that black patients were significantly less likely to undergo transplantation compared to white patients (14% versus 26%;  $P = 0.001$ ). Conversely, black patients were more likely to receive palliative and/or hospice care for HCC (31%

versus 20%;  $P = 0.001$ ). The disparity in transplantation was unchanged when adjusted for age, BMI, comorbidities, liver disease etiology, disease severity, tumor characteristics, insurance status, and history of alcohol use.

When the subgroup analysis was performed evaluating those patients who were within transplant criteria for tumor stage at diagnosis, black patients remained 54% less likely than their white counterparts to undergo liver transplant. The most common reasons in both races for not undergoing liver transplant were alcohol or drug abuse (28%), medical comorbidities and older age (19%), no referral for OLT (15%), and no interest in transplant after referral (10%). In the overall population analyzed, black patients were more likely to have an alcohol abuse history (59% versus 42%;  $P < 0.001$ ), and in the subgroup of patients able to undergo transplant, black patients were significantly more likely than white patients to be declined for transplantation because of drug and alcohol abuse (39% versus 18%;  $P = 0.03$ ). Insurance status did not predict transplant disparity in multivariate analysis, but it is notable that 42% of white patients on Medicaid underwent transplantation compared to 17% of black patients on Medicaid.

The authors attempted to evaluate the complex relationship between race, insurance status, and receipt of a liver transplant through a multivariate stepwise analysis, and despite adjusting for many factors (including other clinical characteristics), they continued to find a significant disparity between black and white patients with regard to liver transplant. These data support the numerous reports that have been published in recent decades that continue to document a racial disparity in health care at multiple levels.

The strength of this study is the in-depth analysis of a large population with HCC. Several population-based studies that have been published using databases, such as the Surveillance, Epidemiology, and End Results database from the National Cancer Institute, have also shown significant racial and ethnic disparities in HCC treatments and outcomes.<sup>(2,6)</sup> These database studies are excellent for supporting findings from single-center studies such as this one but do not allow for per-patient analysis of reasons for certain treatment choices. The study by Dakhouli et al. is from a single transplant center, but Indiana University is the only transplant center in the state and is located in a large metropolitan area. Despite

this strength, there remains a very large referral bias in this study. The authors compared their data with the Indiana State Cancer Registry and estimated that this study captured only approximately 25% of black patients with HCC in Indiana. It is likely that the other 75% of black patients who were not referred to this center could also have contained patients within transplant criteria, and thus the disparity that the authors saw with their data is likely to be even worse when evaluating the entire population of the state. As most transplant centers are within larger cities, this would likely hold true in other states as well.

While this study does not answer all the questions around the reasons for disparity in liver transplant for HCC, it does help to clarify some issues that result in lower rates of liver transplant in black patients. The main issues affecting listing for liver transplant included alcohol and drug use, lack of referral, lack of insurance, financial issues, and lack of interest. While not all these issues are solvable, it is incumbent on the medical community to work to improve health care barriers for access to transplant and other medical care. Educating both providers and patients on issues regarding physician perceptions, referral delays, and patient-level misunderstanding of the outcomes of liver transplant may be a first step in the right direction. We must foster better and more effective physician–patient interactions to improve the quality of care and ensure that we can

overcome the barriers that result in lower access to curative therapies for this deadly disease.

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